

Claims

1. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of at least one of

5 SEQ ID NO.: 2, SEQ ID NO.: 4 and SEQ ID NO.: 6

for use as a medicament.

2. An isolated polypeptide according to claim 1, wherein said amino acid sequence has at
10 least 80% sequence identity to SEQ ID NO.: 2, SEQ IN NO.: 4 and SEQ ID NO.: 6.

3. An isolated polypeptide according to claim 1 or 2, wherein said amino acid sequence is a sub-sequence of with a minimum length of 10 amino acids.

15 4. A polypeptide according to claim 1, wherein said polypeptide comprises the amino acid sequence shown in SEQ ID NO:2.

5. A polypeptide according to claim 4, wherein said polypeptide consists of the amino acid sequence shown in SEQ ID NO:2.

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6. A polypeptide according to claim 1, wherein said polypeptide comprises the amino acid sequence shown in SEQ ID NO:4.

7. A polypeptide according to claim 6, wherein said polypeptide consists of the amino acid
25 sequence shown in SEQ ID NO:4.

8. A polypeptide according to claim 1, wherein said polypeptide comprises the amino acid sequence shown in SEQ ID NO:6.

30 9. A polypeptide according to claim 8, wherein said polypeptide consists of the amino acid sequence shown in SEQ ID NO:6.

10. A polypeptide according to claim 1, wherein said amino acid sequence has at least 80% sequence identity to SEQ ID NO:2.

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11. A polypeptide according to claim 1, wherein said amino acid sequence has at least 80% sequence identity to SEQ ID NO:4.

12. A polypeptide according to claim 1, wherein said amino acid sequence has at least 80% sequence identity to SEQ ID NO:6.
13. An polypeptide to claim 1-12, wherein said amino acid is consistently up-regulated
5 after antibody selection-induced change from VSA_{UM} to VSA_{SM} expression.
14. An polypeptide according to claim 1-13, wherein said amino acid sequence is capable of mediating cyto-adhesion of intact erythrocyte infected by a parasite to human endothelial cells, but not to the CD36 receptor.
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15. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of at least one of
- a) SEQ ID NO.: 1, SEQ ID NO.: 3 and SEQ ID NO.: 5
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- for use as a medicament.
16. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least 80% sequence identity to SEQ ID NO.: 1, SEQ ID NO.: 3 or SEQ ID NO.: 5.
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17. A nucleic acid according to claim 15-16, wherein said nucleotide sequence is a sub-sequence of with a minimum length of 30 nucleotides.
18. A nucleic acid according to claim 15, wherein said nucleic acid comprises the nucleotide
25 sequence shown in SEQ ID NO:1.
19. A nucleic acid according to claim 18, wherein said nucleic acid consists of the nucleotide sequence shown in SEQ ID NO:1.
- 30 20. A nucleic acid according to claim 15, wherein said nucleic acid comprises the nucleotide sequence shown in SEQ ID NO:3.
21. A nucleic acid according to claim 20, wherein said nucleic acid consists of the nucleotide sequence shown in SEQ ID NO:3.
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22. A nucleic acid according to claim 15, wherein said nucleic acid comprises the nucleotide sequence shown in SEQ ID NO:5.

23. A nucleic acid according to claim 22, wherein said nucleic acid consists of the nucleotide sequence shown in SEQ ID NO:5.
24. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least
5 80% sequence identity to SEQ ID NO:1.
25. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least 80% sequence identity to SEQ ID NO:3.
- 10 26. A nucleic acid according to claim 15, wherein said nucleotide sequence has at least 80% sequence identity to SEQ ID NO:5.
27. A nucleic acid sequence according to claim 15-26, wherein said sequence is consistently upregulated after antibody selection-induced change from VSA_{UM} to VSA_{SM}
15 expression.
28. A nucleic acid according to claim 15-17, wherein said nucleic acid sequence encodes a polypeptide which is capable of mediating cyto-adhesion of intact erythrocyte infected by a parasite to human endothelial cells, but not the CD36 receptor.
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29. A recombinant vector comprising the nucleic acid defined in any of claims 15-28 operably linked to one or more control sequences for use as a medicament
30. A composition comprising a polypeptide according to any of claims 1-14 or a nucleic
25 acid according to any of claims 15-28 and a pharmaceutically acceptable diluent, carrier or adjuvant.
31. A composition according to claim 30, wherein said composition is an immunogenic composition.
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32. A composition according to claim 31, wherein said composition induces an IgG/IgM antibody response.
33. An isolated antibody or isolated antiserum induced in response to one or more
35 polypeptides as defined in any of claims 1-14 and/or to one or more nucleic acids as defined in any of claims 15-28.

34. An antibody according to claim 33, wherein said antibody is capable of binding to a molecule expressed on the surface of an intact erythrocyte infected by a parasite causing malaria.

5 35. An antibody according to claim 33, wherein said antibody is capable of recognising parasites selected *in vitro* for expression of VSA_{SM}.

36. An antibody according to claim 33, wherein said antibody is capable of binding to a molecule expressed on the surface of an intact erythrocyte infected by a parasite capable
10 of mediating cyto-adhesion of intact erythrocyte infected by a parasite to human endothelial cells, but not the CD36 receptor.

36. A vaccine comprising at least one nucleic acid according to any of claims 15-28 or at least one vector according to claim 29, the vaccine effecting *in vivo* expression of at least
15 one antigen by a subject, to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to malaria caused by *Plasmodium falciparum*.

37. Use of a polypeptide according to any of claims 1-14 for the manufacture of a
20 composition to be administered in order to prophylactically or therapeutically reduce the incidence, prevalence or severity of malaria in a subject.

38. Use of a polypeptide according to any of claims 1-14 for the manufacture of a vaccine for malaria prophylaxis.

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39. Use of a polypeptide according to any of claims 1-12 for the manufacture of a composition for vaccination against malaria.

40. Use of a nucleic acid according to any of claims 15-28 for the manufacture of an
30 composition to be administered in order to prophylactically or therapeutically reduce the incidence, prevalence or severity of malaria in a subject.

41. Use of a nucleic acid according to any of claims 1-28 for the manufacture of a vaccine for malaria prophylaxis.

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42. Use of a nucleic acid according to any of claims 15-28 for the manufacture of a composition for vaccination against malaria.

43. Use of a recombinant vector according to claim 29 for the manufacture of a composition to be administered in order to prophylactically or therapeutically reduce the incidence, prevalence or severity of malaria in a subject.

5 44. Use of a recombinant vector according to claim 29 for the manufacture of a vaccine for prophylactic treatment of severe malaria.

45. Use of a recombinant vector according to claim 29 for the manufacture of a composition for vaccination against severe malaria.

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46. Use according to any of claims 37-45, wherein said malaria is caused by *Plasmodium falciparum*.

47. A method for prophylactically or therapeutically reduce the incidence, prevalence or
15 severity of malaria in an subject said method comprising administering to said subject an effective amount of a polypeptide according to any of claims 1-14, a nucleic acid according to any of claims 15-28 or a recombinant vector according to claim 29.

48. A method for the prophylactic treatment of severe malaria in an subject, said method
20 comprising administering to said subject an effective amount of a polypeptide according to any of claims 1-14, a nucleic acid according to any of claims 15-28 or a recombinant vector according to claim 29.

49. A vaccination method against severe malaria in an subject, said vaccination method
25 comprising administering to said subject an effective amount of a polypeptide according to any of claims 1-14, a nucleic acid according to any of claims 15-28 or a recombinant vector according to claim 29.

50. A vaccine comprising any of the polypeptides according to any of claims 1-14, the
30 nucleic acids according to any of claims 15-28 or the recombinant vector according to claim 29, said vaccine characterised in that it induces an immune response, wherein said immune response specifically recognises a molecule expressed on the surface of an intact erythrocyte infected by a parasites.

35 51. A vaccine comprising one or more B-cell and/or T-cell epitopes originating from any of the polypeptides according to any of claims 1-14, the nucleic acids according to any of claims 15-28 or the recombinant vector according to claim 29, said vaccine characterised in that it induces an immune response, wherein said immune response specifically

recognises a molecule expressed on the surface of an intact erythrocyte infected by a parasites.

52. A DNA vaccine, which results in the expression of a polypeptide comprising one or
5 more B-cell and/or T cell epitopes from any of the polypeptide sequences according to claim 1-14, wherein said vaccine is capable of inducing an immune response, wherein said immune response specifically recognises a molecule expressed on the surface of an intact erythrocyte infected by parasites.

10 53. A DNA vaccine comprising at least one nucleic acid sequences according 15-28, wherein said vaccine is capable of inducing an immune response, wherein said immune response specifically recognises a molecule expressed on the surface of an intact erythrocyte infected by parasites.

15 54. An *in vitro* diagnostic method, said method comprising contacting a sample with a polypeptide according to any of claims 1-14 under conditions allowing an *in vitro* immunological reaction to occur between said polypeptide and the antibodies possibly present in said sample, and *in vitro* detect the antigen-antibody complexes possibly formed.

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55. An *in vitro* diagnostic method according to claim 54, wherein a disease-state profile for a tested subject is generated by determining the concentration or expression level in a sample of sequences as defined in any of claims 1-14 and/or 15-28.

25 56. An *in vitro* diagnostic kit comprising

a) a sequence as defined in any of claims 1-14 and/or 15-28

b) reagents for preparing a suitable medium for carrying out an immunological reaction between an antibody present in a sample of body fluid or tissue and said sequence; and

30 c) reagents allowing the detection of the antigen-antibody complexes formed, wherein said reagents may bear a radioactive or non-radioactive label.

57. A method for generating a vaccine against severe malaria comprising

35 a) injecting a sequence according to any of claims 1-14 in a subject

b) enabling said subject to generate antibodies specifically recognising any of the polypeptide sequences according to claim 1-14

c) purify said antibodies

d) selecting antibodies having cross-reactivity to parasites causing severe malaria

e) selecting antibodies having the ability to inhibit adhesion to endothelial cells.

58. A method for testing an inhibitor-molecule capable of inhibiting binding of any of the polypeptides according to claim 1-14 to a receptor expressed on endothelia cells

5 comprising

a) *in vitro* cultures of endothelial cells

b) add potential inhibiting-molecule

c) add RBC infected with parasites, said iRBC expressing any of said polypeptide sequences on their surface of the RBC

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d) measure the binding of the iRCB with said endothelia cells by microscopy or other means of quantifying binding as for instance liquid scintillation spectrometry.